

AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions and listing of the claims in the application:

LISTING OF THE CLAIMS:

Claims 1-65 (Canceled)

Claim 66. (Currently amended) An ~~in-vitro~~ in vitro method of making linear sequence variants from at least one heteroduplex polynucleotide wherein said heteroduplex has at least two non-complementary nucleotide base pairs separated by complementary nucleotide base pairs, said method comprising:

- a. preparing at least one heteroduplex polynucleotide, the heteroduplex having first and second strands;
- b. combining said heteroduplex polynucleotide with ~~a defined composition containing enzymes wherein the~~ enzymes consisting essentially of an effective amount of CEL I, T4 DNA polymerase, and T4 DNA ligase;
- c. allowing sufficient time for the percentage of complementarity to increase, wherein one or more sequence variants are made, thereby increasing the diversity in a population of polynucleotides; and
- d. separating and recovering at least one sequence variant having a sequence different from either polynucleotide strand in said heteroduplex.

Claim 67. (Currently amended) An ~~in-vitro~~ in vitro method of making linear sequence variants from at least one heteroduplex polynucleotide wherein said heteroduplex has at least two non-complementary nucleotide base pairs separated by complementary nucleotide base pairs, said method comprising:

- a. preparing at least one heteroduplex polynucleotide, the heteroduplex having first and second strands;
- b. combining said heteroduplex polynucleotide with ~~a defined composition containing enzymes wherein the enzymes consisting~~ essentially of an effective amount of a mismatch recognizing and mismatch directed endonuclease that cleaves at the mismatched nucleotides, an enzyme or enzymes with 3' to 5' exonuclease activity, and an enzyme or enzymes with polymerase activity, ~~and a mismatch recognizing and mismatch directed endonuclease that cleaves at the mismatched nucleotides~~;
- c. allowing sufficient time for the percentage of complementarity to increase, wherein ~~at least one or more sequence variants are made~~, thereby increasing diversity in a population of polynucleotides; and
- d. separating and recovering at least one sequence variant having a sequence different from either polynucleotide strand in the heteroduplex.

Claim 68. (Currently amended) The method of claim 67 wherein said endonuclease is added first, the said enzyme or enzymes having 3' to 5' exonuclease activity is added second, and ~~the~~ said enzyme or enzymes having polymerase activity is added third.

Claim 69. (Previously presented) The method of claim 67 wherein said enzymes having exonuclease activity, polymerase activity, and endonuclease are added concurrently.

Claim 70. (Previously presented) The method of claim 67 in step (b) further comprising ligase activity.

Claim 71. (Currently amended) The method of claim 69 in step (b) further comprising ~~a step of, (d) adding a~~ ligase activity.

Claim 72. (Currently amended) The method of claim 70 wherein said ligase is T4 DNA ligase, ~~E. coli~~ E. coli DNA ligase, or Taq DNA ligase.

Claims 73-77. (Canceled)

Claim 78. (Currently amended) The method of claim 67 wherein said ~~agent~~ enzyme with polymerase activity is T4 DNA polymerase.

Claim 79. (Currently amended) The method of claim 67 wherein said ~~enzyme with both~~ polymerase activity and said 3' to 5' exonuclease activity is are provided by a single enzyme selected from the group consisting of: T4 DNA polymerase, T7 DNA polymerase, ~~E. coli~~ E. coli Pol I [1], ~~or~~ and Pfu DNA polymerase.

Claim 80. (Currently amended) The method of claim ~~67-79~~ wherein said enzyme with both polymerase activity and ~~5' to~~ 3' to 5' exonuclease activity is ~~E. coli~~ E. coli Pol I [1].

Claim 81. (Currently amended) The method of claim 67 wherein said effective amount of said endonuclease, ~~and~~ said exonuclease activity ~~and~~ and polymerase activity and said ligase activity are provided by CEL I, T4 DNA polymerase, and T4 DNA ligase respectively.

Claim 82. (Currently amended) The method of claim 67 wherein said effective amount of said endonuclease, ~~and~~ said exonuclease activity ~~and~~ and polymerase activity, and said ligase activity are provided by CEL I, T7 DNA polymerase, and T4 DNA ligase respectively.

Claim 83. (Currently amended) The method of claim 67 wherein an effective amount of said endonuclease, ~~and~~ said exonuclease activity ~~and~~ and polymerase activity, and said ligase activity are provided by T4 endonuclease VII, T4 DNA polymerase, and T4 DNA ligase respectively.

Claim 84. (Canceled)

Claim 85. (Previously presented) The method of claim 67 wherein complementarity is complete yielding a homoduplex polynucleotide.

Claim 86. (Canceled)

Claim 87. (Previously presented) The method of claim 67 wherein at least 2 different polynucleotide sequence variants are formed and recovered.

Claim 88. (Previously presented) The method of claim 67 further comprising screening or selecting a population of sequence variants for a desired functional property.

Claim 89. (Previously presented) The method of claim 88 further comprising selecting a sequence variant that has a different desired function property from any parent polynucleotide.

Claim 90. (Currently amended) The method of claim 67 wherein said at least one heteroduplex polynucleotide has at least three non-complementary nucleotide base pairs separated by complementary nucleotide base pairs and at least 4 different sequence variants are made.

Claim 91. (New) An *in vitro* method of making linear sequence variants from at least one heteroduplex polynucleotide wherein said heteroduplex has at least two non-complementary nucleotide base pairs separated by complementary nucleotide base pairs, said method comprising:

- a. preparing at least one heteroduplex polynucleotide, the heteroduplex having first and second strands;
- b. combining said heteroduplex polynucleotide with enzymes consisting essentially of an effective amount of a plant-derived mismatch recognizing and mismatch directed endonuclease that cleaves at the mismatched nucleotides, an enzyme or enzymes with 3' to 5' exonuclease activity, and an enzyme or enzymes with polymerase activity;
- c. allowing sufficient time for the percentage of complementarity to increase, wherein at least one or more sequence variants are made, thereby increasing diversity in a population of polynucleotides; and
- d. separating and recovering at least one sequence variant having a sequence different from either polynucleotide strand in the heteroduplex.

Claim 92. (New) The method of claim 91 wherein said endonuclease is added first, said enzyme or enzymes having 3' to 5' exonuclease activity is added second, and said enzyme or enzymes having polymerase activity is added third.

Claim 93. (New) The method of claim 91 wherein said enzymes having exonuclease activity, polymerase activity, and endonuclease are added concurrently.

Claim 94. (New) The method of claim 91 in step (b) further comprising ligase activity.

Claim 95. (New) The method of claim 93 in step (b) further comprising ligase activity.

Claim 96. (New) The method of claim 94 wherein said ligase is T4 DNA ligase, *E. coli* DNA ligase, or Taq DNA ligase.

Claim 97. (New) The method of claim 91 wherein said enzyme with polymerase

activity is T4 DNA polymerase.

Claim 98. (New) The method of claim 91 wherein said 3' to 5' exonuclease activity and said polymerase activity are provided by a single enzyme selected from the group consisting of: T4 DNA polymerase, T7 DNA polymerase, *E. coli* Pol I, and Pfu DNA polymerase.

Claim 99. (New) The method of claim 91 wherein said polymerase activity and said 3' to 5' exonuclease activity are provided by *E. coli* Pol I.

Claim 100. (New) The method of claim 91 wherein an effective amount of said endonuclease is provided by CEL I or SP nuclease.

Claim 101. (New) The method of claim 91 wherein complementarity is complete yielding a homoduplex polynucleotide.

Claim 102. (New) The method of claim 91 wherein at least 2 different polynucleotide sequence variants are formed and recovered.

Claim 103. (New) The method of claim 91 further comprising screening or selecting a population of sequence variants for a desired functional property.

Claim 104. (New) The method of claim 103 further comprising selecting a sequence variant that has a different desired function property from any parent polynucleotide.

Claim 105. (New) The method of claim 91 wherein said at least one heteroduplex polynucleotide has at least three non-complementary nucleotide base pairs separated by complementary nucleotide base pairs and at least 4 different sequence variants are made.